

AMENDMENTS TO THE CLAIMS

1. (Previously Presented) A pharmaceutical composition comprising a nucleic acid containing a nucleotide sequence encoding the primary amino acid sequence GDF-15 protein of the TGF- β superfamily or a functionally active derivative or part thereof having at least a neurotrophic effect on DAergic neurons, wherein the gene coding for the GDF-15 protein of the TGF- β superfamily is transcribed and/or translated in neurons and glial cells, or a vector containing at least the nucleic acid or a protein encoded by the nucleic acid or an antibody or a functional fragment thereof directed against the protein or an antagonist directed to the protein or an agonist as a substitute for the protein, optionally in combination with a pharmaceutically acceptable carrier and/or diluent, for the prevention and/or treatment of neurodegenerative disorders in mammals.

2. (Original) The pharmaceutical composition according to claim 1, wherein the neuron and glial cells are of mammalian origin.

3. (Previously Presented) The pharmaceutical composition according to claim 1, wherein the protein GDF-15 protein of the TGF- β superfamily protects against neurodegenerative events.

4. (Original) The pharmaceutical composition according to claim 3, wherein the neurodegenerative event is mediated by oxidative damage and/or free radical damage and/or mediators and/or executors of neuronal death programs.

5. (Original) The pharmaceutical composition according to claim

4, wherein the mediators of the free radical damage are selected from the group consisting of iron, NO donors, and other free radical donors, and the mediators and executors of neuronal death programs are selected from the group consisting of caspases and pro- and anti-apoptotic members of the bcl-2 family.

6. (Currently Amended) The pharmaceutical composition according to claim 1, wherein the nucleic acid comprises at least the nucleotide sequence shown in Fig. 7A (SEQ ID NO. 1) or the nucleotide sequence shown in Fig. 8A (SEQ ID NO. 2) or nucleotides 40 to 333 of the nucleotide sequence shown in Fig. 8A (SEQ ID NO. 2) or mutants thereof leading to the expression of functionally active polypeptides.

7. (Currently Amended) The pharmaceutical composition according to claim 1, wherein the protein encoded by the nucleic acid comprises at least the primary amino acid sequence shown in Fig. 7B (SEQ ID NO. 3) or the primary amino acid sequence shown in Fig. 8B (SEQ ID NO. 4) or amino acid residues 14 to 111 of the sequence shown in Fig. 8B (SEQ ID NO. 4) as well as homologs thereof having conservative amino acid substitutions.

8. (Previously Presented) The pharmaceutical composition according to claim 1, wherein the mammal is a human.

9. (Previously Presented) The pharmaceutical composition according to claim 1, wherein the neurodegenerative disorders are selected from the group of acute and/or chronic neurological and psychological disorders.

10. (Original) The pharmaceutical composition of claim 9, wherein the neurological and psychological disorders are caused by

stroke, parkinson's disease, Alzheimer's disease or other dementias, infections of the CNS and psychiatric disorders associated with disturbances in CNS transmitter systems.

11. (Original) The pharmaceutical composition according to claim 10, wherein the psychiatric disorders are selected from the group consisting of depression and schizophrenia.

12. (Previously Presented) The pharmaceutical composition according to claim 1, further comprising one or more agents having neurotrophic activity or functionally active derivatives or parts thereof.

13. (Original) The pharmaceutical composition according to claim 12, wherein the agent is a cytokine.

14. (Original) The pharmaceutical composition according to claim 13, wherein the cytokine is selected from the group consisting of GDF, GDNF, TGF, activins, BMP, BDNF, NGF, EGF, CNTF and FGF.

15. (Previously Presented) A diagnostic kit comprising a nucleic acid containing a nucleotide sequence encoding the primary amino acid sequence of a GDF-15 protein of the TGF- β superfamily or a functionally active derivative or part thereof having at least a neurotrophic effect on DAergic neurons, wherein the gene coding for GDF-15 protein of the TGF- β superfamily is transcribed and/or translated in neurons and glial cells, and/or a vector containing at least the nucleic acid and/or a protein encoded by the nucleic acid and/or an antibody or a functional fragment thereof directed against the protein, for the detection of neurodegenerative disorders in mammals.

16. (Original) The diagnostic kit according to claim 15, wherein the neuron and glial cells are of mammalian origin.

17. (Previously Presented) The diagnostic kit according to claim 15, wherein the GDF-15 protein of the TGF- β superfamily protects against neurodegenerative events.

18. (Original) The diagnostic kit according to claim 17, wherein the neurodegenerative event is mediated by oxidative damage and/or free radical damage and/or mediators and/or executors of neuronal death programs.

19. (Original) The diagnostic kit according to claim 18, wherein the mediators of the free radical damage are selected from the group consisting of iron, NO donors, and other free radical donors, and the mediators and executors of neuronal death programs are selected from the group consisting of caspases and pro- and anti-apoptotic members of the bcl-2 family.

20. (Currently Amended) The diagnostic kit according to claim 15, wherein the nucleic acid comprises at least the nucleotide sequence shown in Fig. 7A (SEQ ID NO. 1) or the nucleotide sequence shown in Fig. 8A (SEQ ID NO. 2) or nucleotides 40 to 333 of the nucleotide sequence shown in Fig. 8A (SEQ ID NO. 2) or mutants thereof leading to the expression of functionally active polypeptides.

21. (Currently Amended) The diagnostic kit according to claim 15, wherein the protein encoded by the nucleic acid comprises at least the primary amino acid sequence shown in Fig. 7B (SEQ ID NO. 3) or the primary amino acid sequence shown in Fig. 8B (SEQ ID NO. 4) or amino acid residues 14 to 111 of the sequence shown

in Fig. 8B (SEQ ID NO. 4) as well as homologs thereof having conservative amino acid substitutions.

22. (Previously Presented) The diagnostic kit according to claim 19, wherein the mammal is a human.

23. (Previously Presented) The pharmaceutical composition according to claim 2, wherein GDF-15 protein of the TGF- β superfamily protects against neurodegenerative events.

24. (Previously Presented) The diagnostic kit according to claim 16, wherein the GDF-15 protein of the TGF- β superfamily protects against neurodegenerative events.

25. (Currently Amended) The pharmaceutical composition according to claim 2, wherein:

the GDF-15 protein of the TGF- β

superfamily protects against neurodegenerative events;

the neurodegenerative event is mediated by oxidative damage and/or free radical damage and/or mediators and/or executors of neuronal death programs;

the mediators of the free radical damage are selected from the group consisting of iron, NO donors, and other free radical donors, and the mediators and executors of neuronal death programs are selected from the group consisting of caspases and pro- and anti-apoptotic members of the bcl-2 family;

either the nucleic acid comprises at least the nucleotide sequence shown in Fig. 7A (SEQ ID NO. 1) or the nucleotide sequence shown in Fig. 8A (SEQ ID NO. 2) or nucleotides 40 to 333 of the nucleotide sequence shown in Fig. 8A (SEQ ID NO. 2) or mutants thereof leading to the expression of functionally active polypeptides; or the protein encoded by the nucleic acid

comprises at least the primary amino acid sequence shown in Fig. 7B (SEQ ID NO. 3) or the primary amino acid sequence shown in Fig. 8B (SEQ ID NO. 4) or amino acid residues 14 to 111 of the sequence shown in Fig. 8B (SEQ ID NO. 4) as well as homologs thereof having conservative amino acid substitutions;

the mammal is a human;

the neurodegenerative disorders are selected from the group of acute and/or chronic neurological and psychological disorders;

the neurological and psychological disorders are caused by stroke, parkinson's disease, Alzheimer's disease or other dementias, infections of the CNS and psychiatric disorders associated with disturbances in CNS transmitter systems;

the psychiatric disorders are selected from the group consisting of depression and schizophrenia;

the agent is a cytokine selected from the group consisting of GDF, GDNF, TGF, activins, BMP, BDNF, NGF, EGF, CNTF and FGF; and

further comprising one or more agents having neurotrophic activity or functionally active derivatives or parts thereof.

26. (Currently Amended) The diagnostic kit according to claim 16, wherein:

the GDF-15 protein of the TGF- β superfamily protects against neurodegenerative events;

the neurodegenerative event is mediated by oxidative damage and/or free radical damage and/or mediators and/or executors of neuronal death programs;

the mediators of the free radical damage are selected from the group consisting of iron, NO donors, and other free radical donors, and the mediators and executors of neuronal death programs are selected from the group consisting of caspases and pro- and anti-apoptotic members of the bcl-2 family;

wherein the nucleic acid comprises at least the nucleotide

sequence shown in Fig. 7A (SEQ ID NO. 1) or the nucleotide sequence shown in Fig. 8A (SEQ ID NO. 2) or nucleotides 40 to 333 of the nucleotide sequence shown in Fig. 8A (SEQ ID NO. 2) or mutants thereof leading to the expression of functionally active polypeptides;

the protein encoded by the nucleic acid comprises at least the primary amino acid sequence shown in Fig. 7B (SEQ ID NO. 3) or the primary amino acid sequence shown in Fig. 8B (SEQ ID NO. 4) or amino acid residues 14 to 111 of the sequence shown in Fig. 8B (SEQ ID NO. 4) as well as homologs thereof having conservative amino acid substitutions; and

the mammal is a human.